

**REMARKS**

**1. Amendments to the Claims**

Claims 1 to 71 are cancelled. New claims 72 to 100 have been introduced.

Claim 72 recites treatment of an injury or dysfunction of the central or peripheral nervous system in an animal (which includes a human being, cp. claim 80) by means of antibody which binds to a receptor of the Vps10p-domain receptor family in such manner as to inhibit the binding fo a pro-neurotrophin to such a receptor.

Thus claim 72 narrows claim 1 in several respects

(1) it imposes a requirement of treatment of an injury or dysfunction of the central or peripheral nervous system, per original claim 28;

(2) it requires that the agent be antibody, cp. original claim 12;

(3) it requires that the agent inhibit binding of a pro-neurotrophin to the receptor, cp. clause (ii) of claim 1 and original claim 13 and page 27, liens 11-13; and

(4) it requires that the agent bind to the receptor, cp. clause (i) of claim 1, and original claims 16 and 17.

Claim 73 limits the pro-neurotrophin to pro-NGF, pro-BDNF, pro-NT-3 or pro-NT-4/5, cp. original claim 6.

Claim 74 limits the receptor to the well-characterized receptors SorLA, Sortilin, SorCS1, SorCS2 or SorCs3, cp. original claim 10, and claim 75 limits it further to Sortilin (SEQ ID NO:1).

Claim 78 limits the antibody binding site to an extracellular part of the receptor, cp. original claim 14, and 79 to the cytoplasmic part, cp. page 29, lines 26-33. Claim 76 and 77 limit the antibody binding site on sortilin to particular subsequences of SEQ ID NO:1, cp. original claims 16 and 17. Claim 19 limits the antibody binding site on SorLA to

a particular subsequence of SEQ ID NO:2.

Claim 93 parallels claim 72, but instead of requiring treatment, it simply requires pro-neurotrophin/receptor binding inhibition in an animal suffering from an injury on dysfunction of the central or peripheral nervous system.

## **2. Definiteness Issue**

The Examiner, in items 4-8 of the rejection, rejects claims 1-5, 7, 10-17, 33-37, 40-42 and 45 under 35 U.S.C. § 112, 2<sup>nd</sup> paragraph for failing to particularly point out and distinctly claim the subject matter of the invention.

The language "modulating" and "capable of", criticized in items 5 and 6 of the rejection, have been omitted. In view of the above discussed amendments and the cancellation of previous claims 14 and 15, the invention as currently claimed particularly points out and distinctly claims the subject matter of the invention. Thus the rejections raised in items 4-8 are believed to have been overcome.

## **3. Written Description Issue**

Examiner in items 9-10 of the communication rejects claims 1-5, 7, 10-17, 33-37, 40-42 and 45 under 35 U.S.C. §112, 1<sup>st</sup> paragraph as failing to comply with the written description requirement.

As discussed above, new claim 72 replacing previous claim 1, is directed to an antibody wherein said antibody specifically binds a receptor of the Vps10p-domain receptor family, thereby inhibiting binding of a pro-neurotrophin to said receptor.

Accordingly to the PTO's own Written Description Training Materials, Example 16, a claim to "any antibody which is capable of binding to antigen X" satisfies written description, given merely a teaching of how to make antigen X

(or at least adequate characterization of antigen X) and a suggestion that antibodies can be raised against that antigen.

The recited receptor family is defined at page 24, lines 32-34 and the "pro-neurotrophin" at page 25, lines 15-19. The present specification discloses the complete amino acid sequence of at least five different receptors of the claimed receptor family (SEQ ID NOS:1-5 see pp. 1-2, 8) and these are considered representative of the recited genus of receptors. Should the examiner disagree, there is certainly written description of the sequences (SEQ ID NOS:1-5) of the five specific antigens (receptors) of claim 74, cp page 8, including the sortilin (SEQ ID NO:1) of claim 75.

Hence, the antigen is fully characterized and can be made by recombinant DNA techniques. The specification also suggests particular antibody target subsequences for sortilin and SorLA, see e.g., page 27, line 33 to page 28, line 13, and incorporates by reference Geysen's teaching as to how to screen for epitopes, page 16, lines 33-35, and see also page 18, line 20 to page 19, line 2 for hydrophilicity data and prediction of epitopes thereby. See also page 17, lines 1-5.

According to WDTM Ex. 16, "the general knowledge in the art is such that antibodies are structurally well characterized", the sequence of constant regions is known, and "it is also well know that antibodies can be made against virtually any protein". In the "analysis", the PTO adds

A review of the full content of the specification indicates that antibodies which bind to antigen X are essential to the operation of the claimed invention. The level of skill and knowledge in the art of antibodies at the time of filing was such that production of antibodies against a well-characterized antigen was conventional. This is a mature technology where the level of skill is high and advanced.

The claim is directed to any antibody

which is capable of binding to antigen X.

A search of the prior art indicates that antigen X is novel and unobvious.

Considering the routine art-recognized method of making antibodies to fully characterized antigens, the well defined structural characteristics for the five classes of antibody, the functional characteristics of antibody binding, and the fact that the antibody technology is well developed and mature, one of skill in the art would have recognized that the spectrum of antibodies which bind to antigen X were implicitly disclosed as a result of the isolation of antigen X.

It therefore appears that the present claims satisfy written description.

#### **Enablement Issues**

Examiner in items 9-10 of the communication rejects claims 1-5, 7, 10-17, 33-37, 40-42 and 45 under 35 U.S.C. §112, 1<sup>st</sup> paragraph as failing to comply with the enablement requirement.

Applicants respectfully traverse this rejection for the following reasons.

To satisfy the enablement requirement, the specification need only teach one skilled in the art how to make and use the invention as claimed without undue experimentation.

On page 9 (item 10) of the communication, Examiner states that it would require undue experimentation to discover how to practice Applicant's invention.

The applicant respectfully disagrees. The enclosed declaration signed by Prof. Dr. Willnow outlines the knowledge of the skilled person before the priority date of this application, the contributions made by the present inventors, and certain post-filing evidence of the operability of the instant invention.

The enclosed declaration of Prof. Dr. Willnow, and supporting documents, clearly establish:

- (1) neurotrophins promote survival, differentiation and myelination of neurons and proneurotrophins are processed in vivo into neurotrophins (Declaration §3)
- (2) there is a nexus between modulation of the Vps10p-domain receptor family (which includes sortilin, SEQ ID NO:1) and neurotrophin or pro-neurotrophin activity (Declaration §4)
- (3) there is a nexus between several diseases and agents capable of modulating a receptor of the Vps10p-domain receptor family (Declaration §6)
- (4) it does not require undue experimentation to identify conserved regions of the Vps10p domain receptor, to make antibodies against receptors of that family or against short synthetic peptide fragments of such receptors, to screen such antibodies for the desired binding and inhibitory activity, or to use inhibitory antibodies clinically;
- (5) while the instantaneous pool of sortilin at the cell surface may only be 10%, eventually all sortilin molecules are recycled to the cell surface and exposed to the agents of the present invention (Declaration §5); and
- (6) antibodies can cross the blood-brain barrier, especially when the BBB is made more permeable by certain disease states (Declaration §8).

It is believed that this declaration evidences that the skilled worker would not have required undue experimentation to practice the claimed invention.

Enablement of a generic claim is possible even without a working example, see, e.g., In re Strahilevitz, 212 USPQ 561 (CCPA 1982), and a required screening experiment may yield a small percentage of "hits" yet not be undue experimentation, see In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988); Ex parte Chen, 61 USPQ2d 1025 (BPAI 2000).

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Applicants have further presented new claims which require inhibition of neurotrophin-receptor binding in an animal (including a human) suffering from a nervous system injury or dysfunction, without requiring actual treatment of that injury or dysfunction. Even if the Examiner remains doubtful concerning the treatment efficacy of the recited antibodies, these new claims require only pharmacological inhibition.

Respectfully submitted,

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Enclosure

-Willnow Declaration  
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